Assessment: Nano EHS

Executive Summary

An assessment has been made of the current Measurement Needs (MNs) within Nanotechnology Environmental, Health and Safety (Nano-EHS). It is demonstrated that Nano-EHS is a broad, multi-level, multi-disciplinary sector within the United States Measurement System (USMS). Nano-EHS not only draws from the earlier-assessed Nanotechnology sector, but it also expands upon it to include in particular the biological and environmental implications which must be understood for productive and safe use of nanomaterials. It is also shown that Nano-EHS spans the entire life cycle of a given product, and thus a plethora of Nanotools requirements exist for Nano-EHS.

Analysis demonstrates that there is strong interaction on multiple levels – specifically, Physical, Chemical and EHS characterizations - among the Nano-EHS measurands. Exact details of the measurands and their interactions are of course debatable, but the message is that such measurands do exist and they may need to be considered for a given nano-product. The USMS office here documents the criticality of addressing MNs as a fundamental issue to advancing the nanotechnology community's Nano-EHS understanding.

There were acquired in this assessment a total of 157 MNs (32 measurement needs contributed by expert individuals and 125 roadmap measurement needs identified from earlier authenticated roadmaps, workshops and/or white paper publications). This pool of data was entered into a single, commonly formatted spreadsheet to afford an apples-to-apples comparison among multiple MNs in the Nano-EHS sector. All MNs were authenticated as in the prior USMS assessment. Highlights from the subsequent Analysis include the following:

- Preliminary assessment indicates that Nano-EHS is still early in its R&D time continuum.
- Measurement Needs information in the Roadmaps is often quite general.
- A significant number of MNs indicate a need for instrumentation that can handle complexity and scale beyond current limits.
- A convergence among multiple levels, organizations and disciplines is needed to address many of the Nano-EHS measurement needs; the infrastructure for this convergence may not exist currently.
- The lack of clarity and consensus of terminology definitions can be impediments to a common understanding across disciplines, *e.g.,* toxicologists and materials scientists.
- There exists a common thread among almost all the roadmaps and researchers in the types of MNs being requested; differences lie in the details, *e.g.,* how a specific nanomaterial is measured. The next level of measurement needs assessment may be in these details.

Future efforts from the NIST USMS office will focus upon stimulating more extensive partnerships to build further upon this work, developing web portal pages to further disseminate this information on the USMS website (http://usms.nist.gov), and directing potential measurement solutions to the identified and authenticated measurement needs. Industrial and government partners are forming a working group of Nano-EHS specialists to plan the most expeditious and successful solutions to these critical MNs; interested parties should contact Ms. Clare Allocca (Chief, USMS, clare.allocca@nist.gov).

I. Description of new analysis

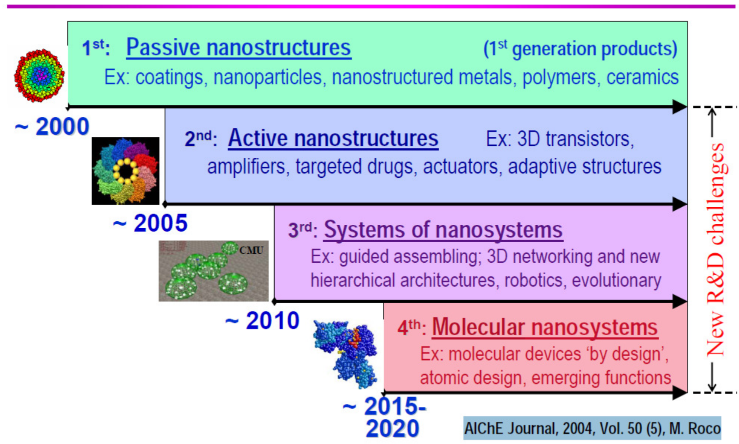
Achieving sustainable development, in which detrimental implications to the Environment, human and animal Health, and occupational Safety (EHS) are minimized, is a core challenge to our society as technology rapidly develops. Manufacturing processes must be designed with EHS considerations front and center, or serious consequences involving chronic disease, injury and even death can potentially result. Moreover, products developed today must be reliable to the point that their manufacturers avoid not only bad press, but also litigation due to their potential failure. These increasingly stringent requirements are even further compounded as new materials with unproven pedigrees in real life applications are proposed as solutions to technical problems.

Nanotechnology is a research sector that particularly requires a better appreciation of its potential EHS implications. The advent of nanotechnology has opened new vistas for many products; however nanomaterials themselves can have unique and potentially hazardous EHS implications because of their size. What is EHS compatible at the macroscale may not be at the nanoscale. Concomitantly, the potential for development of nanomaterials with unknown hazardous properties raises a strong need for improved capabilities of the measurement of nanomaterials, *i.e.,* nanometrology.

A further justification for more aggressively seeking measurement solutions for Nano-EHS issues is the constant evolution of nanotechnology. Roco (2004)[1] presented a timeline for the development of nanotechnology its incipient stage in passive nanostructures through its fully mature stage of molecular nanosystems – see . This maturation of the field of nanotechnology spurs us to seek higher quality instrumentation to provide a better understanding of more complex systems. Moreover, it has been shown by the Woodrow Wilson International Center for Scholars[2] that there are already some 800+ consumer products utilizing nanomaterials available today in the marketplace. To stay ahead of this wave of commercialization development, it is imperative that we proactively assess the measurement needs in Nano-EHS and plan accordingly for developing measurement solutions.

To come to a better understanding of these measurement needs and their potential solutions, an assessment of Nano-EHS measurement needs (MNs) and roadmap measurement needs (RMNs) was undertaken by the National Institute of Standards and Technology's United States Measurement System (NIST's USMS) Office. It is the goal of this assessment to provide the United States - and the world in general - with a resource and the opportunity

Figure 1. Timeline for beginning of industrial prototyping and nanotechnology commercialization: Four Generations.[1]



[1] AIChE Journal, 2004, 50 (5), M. Roco.

[2] http://www.nanotechproject.org/inventories/consumer/

to improve strategic planning so that humanity can safely use the suite of promising nanomaterials already being intensely researched and applied in various products.

a. Nano-EHS Terminology

Challenges in Nano-EHS abound, beginning with the definitions of each term. A set of potential fundamental definitions may be found in Figure 2[3]. It is striking how broad even these preliminary definitions are – an assessment of EHS is thus inherently an interdisciplinary endeavor.

***Nanoscience* involves research to discover new behaviors and properties of materials with dimensions at the nanoscale which ranges roughly from 1 to 100 nm. *Nanotechnology* is the way discoveries made at the nanoscale are put to work. Nanotechnology is more than throwing together a batch of nanoscale materials-it requires the ability to manipulate and control those materials in a useful way.**

Environment – air, soil, water, and other media that make up the world in which we live

Health – general condition of the body, including both human and animal

Safety – protection from harm to the worker in the occupational environment and the general populace in living places

Figure 2. Nanoscience, Nanotechnology and EHS definitions[3].

There is of course work actively being done on terminology of nanotechnology. For example, within the International Standards Organization resides a Technical Committee 229 (ISO/TC229) on Nanotechnology. Within ISO/TC229 is Joint Working Group 1 (WG1) that is focused on concretely establishing the terminology and nomenclature for nanotechnology activities. ISO/TC229/WG1 has international participation that is making headway in assigning rigorous definitions for a large number of terms. NIST also leads parallel standards and reference materials work (*e.g.,* gold nanoparticle reference materials recently made available) to support these critical efforts. To set the stage for the analysis in this report, we have attempted to define all major relevant Nano-EHS terms in Appendix A. Certainly, the exact definitions are debatable at this writing, but the presented definitions will at least get us started.

b. Nano-EHS Scope

Achieving an understanding of the Nano-EHS sector and particularly the Nanotools needed to assess a nanomaterial's influence upon EHS is becoming a critical issue. As stated in the NNI Strategy for Nano-EHS[4], "Nanotechnology-related environmental, health, and safety (EHS) research is an essential component of the NNI's coordinated research framework. EHS research is focused in particular on understanding general mechanisms of biological interaction with nanomaterials." This is particularly true when one considers the life cycle of a given nanomaterial. As shown in Figure 3, nanomaterials synthesis (the "cradle") precedes the implementation of all nano-products. Nanoproducts themselves can take many forms, as shown with the example icons for pills (nanomedicine), a tennis racquet (sporting goods), a TV (flat screens), an airplane (aerospace industry) and a semiconductor chip (semiconductor industry). Eventually, all nano-products will reach the end of their life cycle (the "grave") and need to be

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[3] The definitions of Nanoscience and Nanotechnology are taken from the National Nanotechnology Initiative – http://www.nano.gov. EHS definitions are given merely as examples to introduce the concept of EHS. Note that there still remains a debate about the exact definition of EHS – see Appendix A, Terminology.

[4] The National Nanotechnology Initiative, "Strategy for Nanotechnology-Related Environmental, Health & Safety Research", February 2008 (http://www.nano.gov).

disposed or recycled. In some nanomaterials, there may be the potential for re-use. Throughout a given nanomaterial's life, however, there is the need to measure its characteristics, performance, and change in properties if relevant. Nanotools are thus needed throughout the life cycle. *Correspondingly, Nano-EHS measurement issues straddle the entire life cycle of a given nanomaterial.*

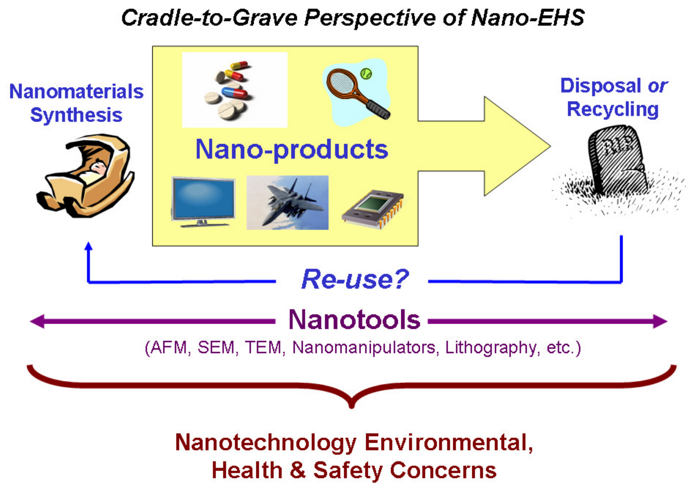


Figure 3. Life-cycle (cradle-to-grave) concerns for nanomaterials. Nano-EHS issues straddle the entire life cycle.

A further complication to the Nano-EHS picture is that there exist a large number of properties that may need to be measured for a given nanomaterial- see Appendix A for preliminary definitions. In the early stages of the measurement needs assessment, it was seen that there are conflicting visions about what Nano-EHS truly is. In an effort to make a clear assessment of Nano-EHS MNs, it was decided to attempt to capture Nano-EHS in a single visual. Figure 4 is the final result after several iterations. This figure (explained in detail below) has been vetted through numerous seminar and workshop presentations, and accordingly updated and corrected to its final form as shown. It offers a holistic perspective on Nano-EHS that was lacking in the nanotechnology community.

Within the nanotechnology community, there are essentially two major camps of researchers: (1) those with a physical science/engineering bent (*e.g.,* chemists, materials scientists, engineers as shown in the upper left in Figure 4), and (2) those with a biological bent (*e.g.,* toxicologists, biologists, geologists as shown in the upper right in Figure 4). To pursue their respective research areas, these groups typically need to acquire different knowledge. The physical science/engineering people seek information on chemical properties, physical properties, quality of materials synthesis, and interactions among the physical and chemical properties. The biological researchers typically need answers on how nanomaterials interact with the environment, how they affect health conditions, what implications they have for safety, and overall what EHS interactions they possess.

Because of these differing needs, each group naturally has different measurement needs. Once a nanomaterial is synthesized - prior to its actual use in a product - the first sets of characterizations typically sought by the physical sciences/engineering researchers encompass those of ***Interrelated Material Properties* –** see Figure 4. Because of the nature of the properties sought, the characterizations listed are highly interrelated - *e.g., Effect of chemical modifications* can affect *Solubility* can affect *Dispersion*.[5]

[5] Note that there is also an *Undefined* category in both the EHS and the Materials Properties bubbles. This is necessary, since several of the submitted Measurement Needs and Roadmap Measurement Needs were too broad to classify into specific measurand buckets. More details follow on this issue.

But even with this set of measurands documented, we still do not have the full story of the nanomaterials interactions with our world. In the early days of nanotechnology (*e.g.*, before the visualization of carbon nanotubes in 1991), characterizations typically stopped at the physical and the chemical. However, as more products are produced for applications in areas such as nanomedicine, it becomes critical to assess not only the physical and chemical nature of the nanomaterial, but also its influence upon EHS. Thus, biological researchers typically seek a second set of properties in Figure 4 that we shall call ***Interrelated EHS Characterizations***. EHS measurements comprise the full suite of biological and environmental measurands[6], which inform us how a material will behave in the environment, in health conditions (both human and animal), and in safety situations (both industrial and general populace). Again, these properties are highly interrelated – *e.g., Metabolic Pathway* can affect *Transport* can affect *Clearance*.

The wall between physical/chemical and EHS characterizations is moreover thin, since *Interrelated EHS Properties* can interact with the *Interrelated Materials Properties*. This is particularly true within *in vivo* situations. For example, even if a set of carbon nanotubes is fully characterized for its physical and chemical characteristics, these properties may change once the CNTs are inserted into living tissue. CNTs may change their agglomeration state, chemical functionalization, *etc.*, as they interact with biological organisms. Essentially, we can consider the permutations infinite for the interactions among multiple measurands. To capture this important point, Figure 4 shows a double-arrow between the *Interrelated EHS Properties* and *Interrelated Materials Properties*. Also shown is a chain between these categories to indicate that there is a strong dependency between the two characterization sets.

Thus, a major challenge in nanotechnology today is the interdisciplinary nature of measurement technology. To have a full understanding of how a given nanomaterial interacts with the macroscopic world, it is important to measure both interrelated material *and* EHS properties. Collaboration across the dotted line shown in Figure 4 will become more and more important as nanomaterials are developed into more complex systems.

Ultimately, the goals of any nano-characterization are envisioned as two-fold in Figure 4, lower left & right: (1) we want to understand the nanomaterial well enough to be confident to have a sufficient understanding of its EHS issues, and thus to enable determination if a nanomaterial is good or bad relative to EHS considerations, and (2) to create internationally recognized standards protocols and reference materials. Achieving such a knowledge base would truly enable nanomaterials far more than they are today.

In short, Nano-EHS has stringent and even dynamic measurement needs. A firm understanding of Nano-EHS is a requirement for the nanotechnology community to move forward with applications which are biologically and environmentally benign, and research and industrially safe.

[6] Measurand – a property of the nanomaterial to be characterized

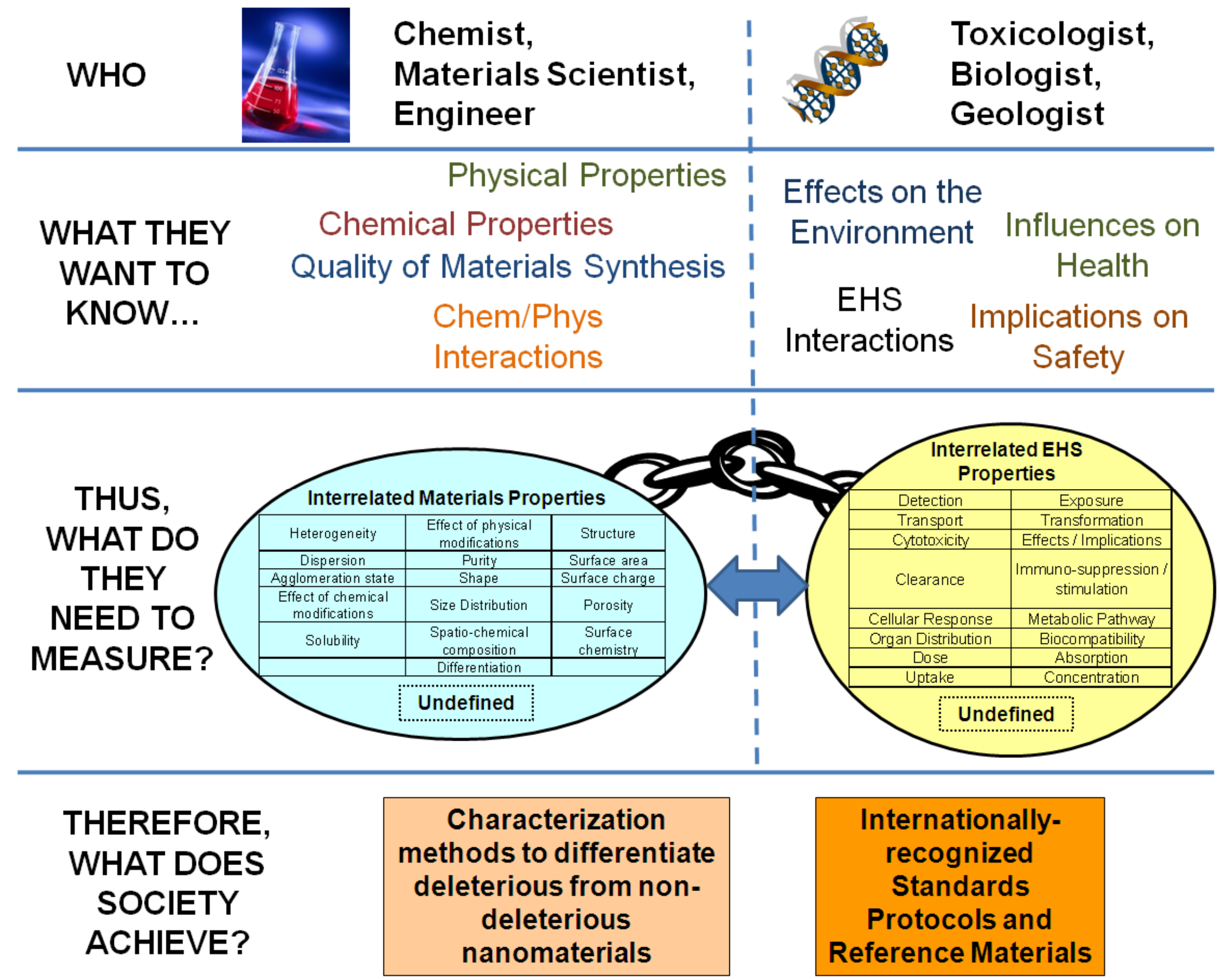


Figure 4. Scope of Nano-EHS characterization requirements.

II. Methodology for Analysis

A key challenge throughout the USMS survey was to engage an interdisciplinary set of scientists/engineers and to review a wide range of roadmaps/white papers/workshop reports to obtain an accurate representation of the field. Toward this end, there were a total of 28 roadmaps, white papers and workshop reports reviewed in detail to obtain the complete set of MNs and RMNs (see *Appendix B*). USMS staff attended numerous workshops/conferences to present the USMS mission and engage nanotechnology researchers and industrial representatives toward their submission of MNs. Consolidation and analysis of all this information was a critical effort.

Once the MNs were acquired with the various categories, we had a dataset that could be analyzed. As documented in the initial USMS assessment, the analysis was based on:

- An analysis of all measurement needs
- Knowledge of the USMS
- Characterization of the USMS

- Published information and data

The data-driven analysis of measurement needs is based on RMNs and individual MNs. First, the published science and technology roadmaps were reviewed. 90% of the roadmaps reviewed in the Nano-EHS sector identified RMNs. The RMNs were analyzed and summarized in a master spreadsheet. This analysis includes all the RMNs as well as RMN subsets. Trends in measurement needs as well as commonalities across sectors and processes/products were identified. All MN and RMN sources are listed in *Appendix B*. Secondly, individual MNs were developed for Nano-EHS using a pre-defined template.

Each MN was then "Tagged" according to pre-defined categories and the results were entered into the master MN database. Building upon the original set of Tags[7], we also incorporated into the Nano-EHS assessment Tags for identifying which of the measurands in Figure 4 were relevant for a given MN. A MN data analysis was then conducted based on all the MN Tags.

III. Results & Discussion

Once the MNs[8] were assembled into a master spreadsheet, the USMS Office ran an analysis upon the results. From this information, we were able to assess the state of the art for MNs in Nano-EHS. These results are presented here. It should be noted that although quantitative results are presented, there is little focus on the actual absolute values of any of the numbers presented in this analysis. The important implications of this analysis are the trends, as discussed.

A. Measurands

A measurand is a property of a material to be measured, such as purity. A key result of the tagging activity is the frequency of measurand occurrence; such data analysis could give us insight into what are the critical needs for new measurement instrumentation within the Nano-EHS sector. Figure 5 presents the preliminary findings from the tagging effort. Of the 157 MNs submitted, there are actually 233 total instances of Measurand tagging – such is the case because numerous times more than one Measurand is assigned to a single MN.

Particularly striking about Figure 5 are the distributions among not only the Measurands, but also their categories according to Figure 4. Although *Materials* has the most assigned Measurands (at 42% of the total count – see pie chart in Figure 5), there were a total of 62 *Uncategorized* Measurands (at 26% of the total count), and 58 of these are classified as *Undefined*. As mentioned earlier, an Uncategorized Measurand is one which cannot be assigned to a single Measurand because of the lack of specificity within the MN itself. We may therefore draw a few preliminary conclusions:

- A theme among the Roadmaps is a need for greater specificity in their MN descriptions.
- The basic research needed to address Nano-EHS MNs is not yet done.
- The largest category is Undefined, which in and of itself is quite telling - we need a better understanding of the basic process and scaling.

[7] "An Assessment of the United States Measurement System: Addressing Measurement Barriers to Accelerate Innovation", Appendix F-The Methodology of the Inferential Analysis, NIST Special Publication 1048, June 2006.

[8] For purposes of brevity, we shall call MNs and RMNs from now on simply MNs.

- Materials Measurands appear to be the strongest message as of this writing from among the Nano-EHS community, although EHS Measurands are close behind
- Aside from the Undefined Measurand, the top five Measurands are, in descending order: Exposure, Spatio-chemical composition, Size distribution, Shape, and Cytotoxicity. This is important to recognize from the perspective of allocating funding and strategic planning in general.

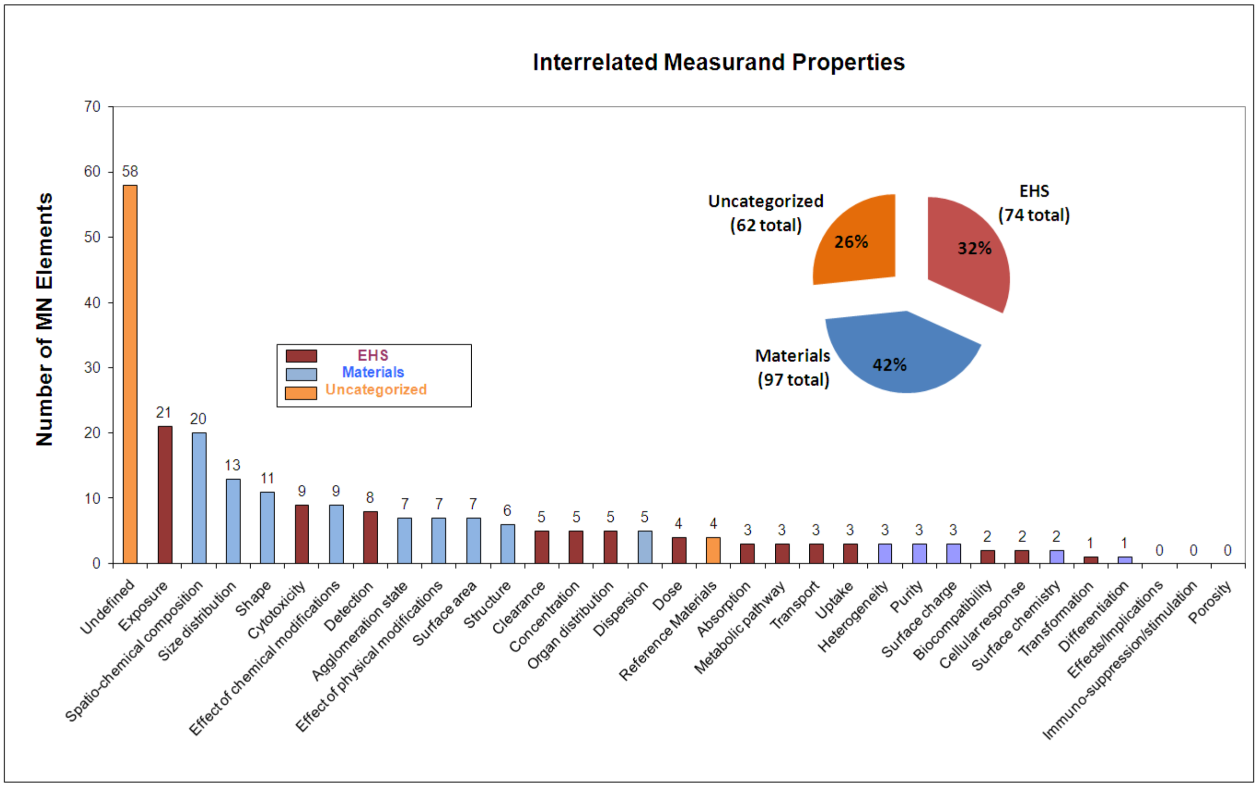


Figure 5. Pareto chart assessment of measurement needs according to the Measurands presented in Figure 4.

B. Measurement Barriers

Within the context of these Measurands in Figure 5, there are Measurement Barriers which impede their solutions. Figure 6 presents a chart of these Measurement Barriers relative to their frequency among all the Measurement Needs. Several of the Measurement Barriers that could be ascribed to early-stage research are most prominent: Accuracy, Reliability, Systems-Level, and Lack of Fundamental Knowledge. Later-stage barriers which one would typically relegate falling into a manufacturing environment (Usability category) – such as Acceptability, Speed, Workforce, Production Readiness, *etc*. – are lesser in number. Measurement Solutions for Nano-EHS MNs thus still have many fundamental technical issues to overcome before they are resolved. From the aggregated perspective, those Measurement Barriers which are classified as posing Technical Limits far outnumber in population those of Usability or General Challenges concerns – see pie chart in Figure 6.

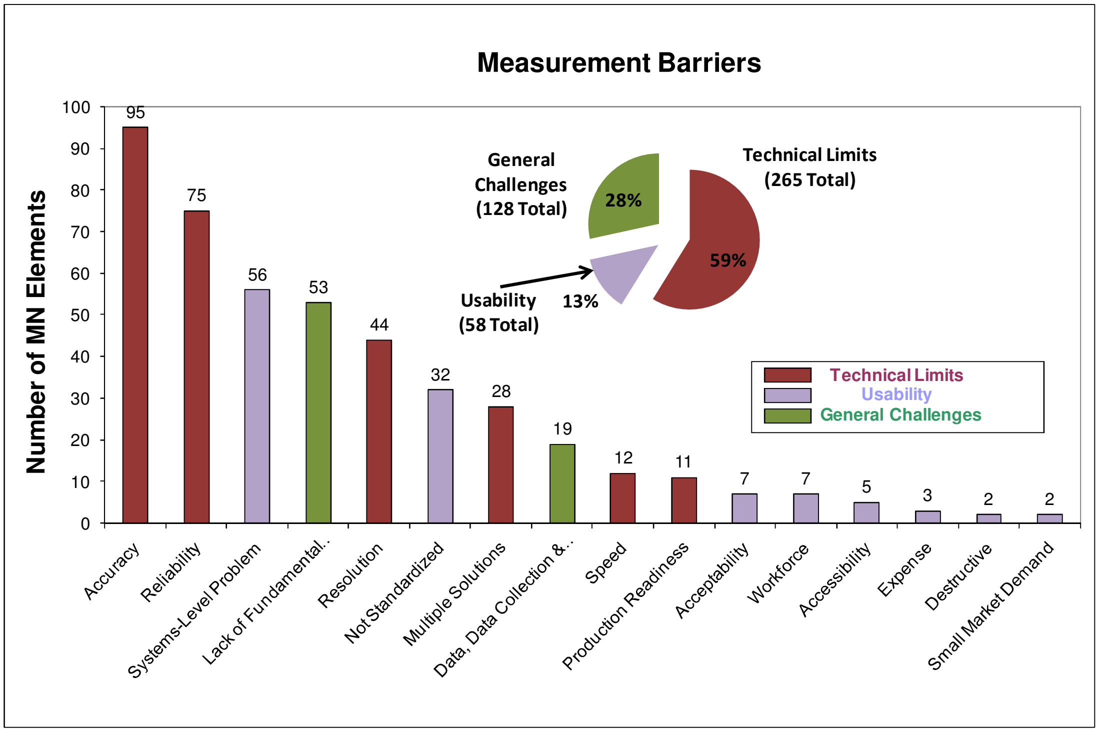


Figure 6. Pareto chart assessment of Measurement Barriers within Nano-EHS.

C. Measurement Solutions

In this work, we have identified the critical MNs for Nano-EHS; however, this is only part of the process. To really provide a value-added contribution to society, we should also start to assess possible *Measurement Solutions* for these MNs. Building upon an earlier report section by Craig Wall (Agilent Technologies, Inc.) and the author Tom Campbell that details characterization equipment for nanocomposites[9], we have created a categorization of major characterization techniques at the nanoscale – Figure 7. Existing instrumentation is grouped according to major categories – *e.g.,* all electron microscopes are clustered under Microscopy. Figure 7 thus offers a snapshot of instrumentation now available as possible Measurement Solutions for Nano-EHS.

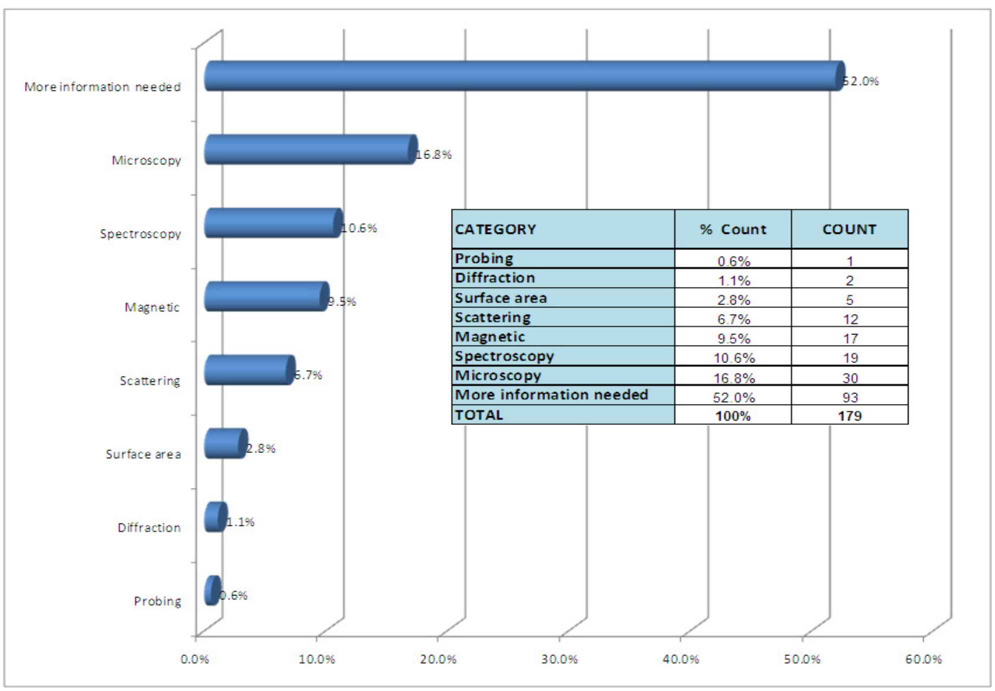
Based upon Figure 7, we then assigned every MN a possible Measurement Solution. From that dataset, we graphed the frequency of occurrence of a given category of characterization equipment for addressing Nano-EHS MNs – see Figure 8. It is striking that more than 50% of the MNs fall into the category of "More information needed". This is, however, right in line with the early nature of the resolution of these MNs. We simply do not have enough knowledge of what we are seeking to assign existing instrumentation to solve most of today's existing MNs.

Generating Measurement Solutions will be a challenge, but it is one that the NIST USMS Office is addressing head-on. Through extensive contacts within the nanometrology vendor community, we are forming a new working group of potential solution providers. The MNs are being openly shared with this group, and a dialogue is beginning on how we may most expeditiously start to address the most critical of the MNs.

[9] "Interagency working group on manufacturing research and development – instrumentation, metrology, and standards for nanomanufacturing", Sponsors: NIST, US Department of Commerce, NSF, Office of Naval Research.

Major Characterization Equipment Categories								
Conductivity (electrical, thermal)	Conductivity Meter							
Diffraction	XRD (X-ray diffraction)	Neutron Diffraction	Electron Diffraction					
Magnetic	Magnetometer	MRI (magnetic resonance imaging)	NMR (nuclear magnetic resonance)					
Microscopy	SPM (scanning probe microscopy)	STM (scanning tunneling microscopy)	NSOM (scanning near field optical microscopy)	TEM (transmission electron microscopy)	STEM (scanning transmission electron microscopy)	SEM (scanning electron microscopy)	CLSM (confocal laser scanning microscopy)	
Probing	Nanoprobe (multiprobe electrical measurements and sample manipulation)	Nano-indentor						
Scattering	SANS (small angle neutron scattering)	SAXS (small angle X-ray scattering)						
Spectroscopy	XAS (X-ray absorption spectroscopy), which includes XANES (X-ray absorption near edge structure) and EXAFS (extended X-ray absorption fine structure)	XPS (X-ray photoelectron spectroscopy) also known as ESCA (electron spectroscopy for chemical analysis)	AES (Auger electron spectroscopy)	SIMS (secondary ion mass spectrometry)	FT-IR (Fourier transform infrared spectroscopy)	Raman Spectroscopy	EDS & WDS (energy dispersive spectroscopy); (wavelength dispersive spectroscopy)	EELS (electron energy loss spectroscopy)
Surface area	BET							

Figure 7. Major categories of characterization equipment toward an assessment of possible Measurement Solutions for Nano-EHS Measurement Needs.



CATEGORY	% Count	COUNT
Probing	0.6%	1
Diffraction	1.1%	2
Surface area	2.8%	5
Scattering	6.7%	12
Magnetic	9.5%	17
Spectroscopy	10.6%	19
Microscopy	16.8%	30
More information needed	52.0%	93
TOTAL	100%	179

Figure 8. Frequency of occurrence of possible Measurement Solution categories from Figure 7 for all Nano-EHS Measurement Needs. Because several MNs had multiple possible Measurement Solutions, total possible Measurement Solutions count is greater than the total MN count.

IV. Conclusions

The NIST USMS Office here presents an assessment of the state of the art of Nanotechnology Environmental, Health and Safety (Nano-EHS) Measurement Needs (MNs). We find several implicit characteristics of Nano-EHS MNs through this effort – to whit:

- Preliminary assessment indicates that Nano-EHS is still early in its R&D time continuum
- Measurement Needs information in the Roadmaps is often quite general.
- A significant number of MNs indicate a need for instrumentation that can handle complexity and scale beyond current limits.
- A convergence among multiple levels, organizations and disciplines is needed to address many of the Nano-EHS measurement needs; the infrastructure for this convergence may not exist currently.
- The lack of clarity and consensus of terminology can be impediments to a common understanding across disciplines, *e.g.,* toxicologists and materials scientists.
- There exists a common thread among almost all the roadmaps and researchers in the types of MNs being requested; differences lie among the details, *e.g.,* how a specific nanomaterial is measured. The next level of measurement needs assessment may be in these details.

Finally, we note that Figure 4 is a sound assessment of the scope of Nano-EHS, and it supports the final conclusions.

Appendix A - Terminology

As was clear at various workshops throughout 2008, it is difficult to make analysis trustworthy without a consensus on definitions. However, achieving consensus on terminology is a challenging effort. The ISO/TC229/WG1 effort on Terminology and Nomenclature is "expected to be long term"[10], in particular because it first requires a basic system of nomenclature. Particularly during the *Environmental, Health and Safety Issues in Nanomaterials* workshop held in Crystal City, VA on June 9-10, 2008, it was noted that it is important to have a baseline set of terminology that people agree to. However, this opportunity is itself clouded by the differing opinions of what even Environment, Health and Safety means. For example, during the June workshop, the below bulleted definitions were obtained from a simple poll of the workshop participants. Clearly, there is a lack of consensus among the experts today.

Environment

Releases into Environment
Environmental Fate
Detection (difficult even in products when at ~1%)
Length scales / transport
TSCA Definition (being redefined currently)
Persistence
Differentiation between naturally occurring and engineered nanomaterials
Background assessment
Water, Soil, Air, Animals
Seasonal or time dependence
Proximity to source
What about nano makes this different?
Intentional *vs*. Accidental Release
Recycling and/or disposal
Remediation (both intentional/unintentional release)
Sustainability
Releases associated with processing?
Releases during consumer use
Traceability
Prediction (including modeling)

Health

Impact on environment and public health from industrial processes
Exposure
Implication / impact / exposure because of workplace
Workplace, environment & consumer
Toxicology (enabling)
Applications *vs*. implications (e.g. drug delivery is application)
Prediction (including models)
Epidemiologist

[10] C. Teague, "Environmental, Health, & Safety Issues in Nanomaterials: Progress in Documentary Standards", Environmental, Health and Safety Issues in Nanomaterials, Crystal City, VA, June 9-10, 2008.

Safety
Corrosivity
Explosivity
Flammability
MSDS guidance – if you should not put CNT under graphite, where should you put them?
Physical implications
Misuse *vs*. Appropriate Use
Product / consumer safety? (then would include toxicity, *etc*.) – means something different to clinician *vs*. process engineer
Reactivity
Engineering controls effectiveness (*e.g.,* to prevent release of too much aerosol)

Despite this lack of consensus in terminology, we as a technical community should still be able to at least posit preliminary definitions for the major terms. Below is a list of terms and their respective definitions that the USMS Office deems as critical to the clarification of the Nano-EHS sector. Respective definitions were taken from multiple sources - including Merriam-Webster's Online Medical Dictionary[11] and Wikipedia[12] - and tailored to the Nano-EHS sector. A key future effort must be to achieve consensus within the international community for these terms.

As related to physical/chemical characterizations

***Agglomeration state* –** a condition in which a cluster of disparate nanomaterials collects together

***Dispersion* –** the spreading or distribution of a nanomaterial from a fixed or constant source

***Effect of chemical modifications* –** changes to the chemical structure of a given nanoparticle, *e.g.,* a chemical functionalization on the external ring of a carbon nanotube

***Effect of physical modifications* –** changes to the physical structure of a given nanoparticle, *e.g.,* an atomistic defect created in a carbon nanotube, since an atomistic defect can change bonding type

Heterogeneity - consisting of dissimilar or diverse ingredients or constituents

***Porosity* –** the distribution of small interstices in a nanomaterial admitting absorption or passage of other material

Purity – the quality or state of being unmixed with any other matter

***Shape* -** the visible makeup of a particular nanomaterial

***Size distribution* –** the variation in physical dimensionality (x,y,z) of a collection of nanoparticles, *e.g.,* a Gaussian curve distribution of carbon nanotube length

***Solubility* -** the amount of a substance that will dissolve in a given amount of another substance; typically expressed as the number of parts by weight dissolved by 100 parts of solvent at a specified temperature and pressure or as percent by weight or by volume

***Spatio-chemical composition* –** the compositional characteristics defining spatially-derived properties (*e.g.,* shape, structure, *etc*.) and chemical properties (*e.g*., functionalization)

[11] http://www.merriam-webster.com/medical/
[12] http://en.wikipedia.org/

Structure - the arrangement of particles or parts of a nanomaterial

Surface area **-** the exposed amount of area on the exterior of a nanomaterial

Surface charge **–** the electric charge present at an interface of a nanomaterial

Surface chemistry **-** the study of chemical reactions at material interfaces

<u>As related to EHS characterizations</u>

Biocompatibility **-** the condition of being compatible with living tissue or a living system by not being toxic or injurious and not causing immunological rejection

Cellular Response - the activity or inhibition of previous activity of a cell or any of its parts resulting from stimulation

Clearance **-** the volume of a nanomaterial that could be freed of a specified constituent in a specified time by excretion of the constituent into the urine through the kidneys—called also *renal clearance*

Cytotoxicity **–** the characteristic of being toxic (inherently harmful) to cells

Detection **–** the determination of the physical presence of a nanomaterial in another media

Effects / Implications **–** the long-term influences of a nanomaterial upon the environment, health and safety of a given media

Exposure **-** the condition of being subject to some detrimental effect or harmful condition; *e.g.,* repeated *exposure* to nanomaterials causing bronchial irritation

Immuno-suppression / stimulation **-** suppression or stimulations (as by drugs) of natural immune responses

Metabolic pathway **-** the sequence of usually enzyme-catalyzed reactions by which one substance is converted into another

Organ distribution **–** the position, arrangement, or frequency of occurrence (as of the members of a group) over an area or throughout a space or unit of time of a selection of nanomaterials among internal organs *in vivo*

Transformation **–** an act, process or instance of being modified from one substance to another, *e.g.,* a cell is *transformed* from benign to cancerous

Transport – an act or process of conveying a nanomaterial from one location to another, especially *in vivo*

<u>As related to Measurement Barriers</u>

Acceptability – the ability of a measurement solution to be accepted by the user community

Accessibility – the ability of a measurement solution to be accessible to the user community

Accuracy – the degree of conformity of a measure to a standard or a true value

Data, data collection & retrieval – the systematic accumulation of data from a measurement solution

Destruction – the need in executing a measurement solution to destroy the given nanomaterial sample, thus limiting measurement reproducibility

Expense – the cost of a given measurement solution relative to other solutions

Lack of fundamental knowledge **–** the state in which there is insufficient knowledge about the basic properties or approaches to measure them of a given nanomaterial

Multiple solutions **–** the state in which there may be more than one measurement solution for a given measurement need

Not standardized **–** the situation in which there is a lack of standardization for the application and measurement technology of a given nanomaterial

Production readiness **–** the condition in which a given measurement solution is ready for use in industry

Reliability - the extent to which a measuring procedure yields the same results in repeated trials

Resolution - the process or capability of making distinguishable the individual parts of an object

Small market demand **–** the property of lacking a significant commercial market for a nanoproduct

Speed **–** the state in which a given measurement can be made rapidly and repeatedly over a short period of time, especially to accommodate industrial processes

Systems level problem **–** a problem in which more than one type of (or too broad of) a measurent need is identifed

Workforce **–** the employable base of people for a given task

Appendix B - Sources

The USMS Office gratefully acknowledges the following contributors (in no particular order) to this assessment of Nano-EHS measurement needs. This work would simply not be possible without their contributions. Roadmaps, white papers and workshop reports that were reviewed also follow.

- Vasgen Shamamian, Dow Corning
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- Lori Goldner, NIST

Assessment: Nano EHS

	Roadmap	Weblink
1	NASA's Microgravity Fluid Physics Strategic Research Roadmap	http://gltrs.grc.nasa.gov/reports/2004/TM-2004-212914.pdf
2	Chemical Industry R&D Roadmap for Nanomaterials By Design	http://www.chemicalvision2020.org/pdfs/nano_roadmap.pdf
3	Nanotechnology and the Environment: Applications and Implications STAR Progress Review Workshop	http://es.epa.gov/ncer/publications/workshop/nano_proceed.pdf
4	Nanoscale Science and Engineering for Agriculture and Food Systems	http://www.nseafs.cornell.edu/web.roadmap.pdf
5	NIH Roadmap for Medical Research	http://nihroadmap.nih.gov/
6	Nanobiotechnology	http://www.nano.gov/nni_nanobiotechnology_rpt.pdf
7	Nanotechnology Innovation for Chemical, Biological, Radiological, and Explosive Detection and Protection	http://www.wtec.org/nanoreports/cbre/CBRE_Detection_11_1_02_hires.pdf
8	Assessment Study on Sensors and Automation in the Industries of the Future	http://www.eere.energy.gov/industry/sensors_automation/pdfs/doe_report.pdf
9	Vision 2020 Materials Technology Roadmap	http://www.eere.energy.gov/industry/chemicals/pdfs/materials_tech_roadmap.pdf
10	Nanotechnology	http://www.technology.gov/reports/TechPolicy/Nanotech/030523.pdf
11	International Technology Roadmap for Semiconductors	http://www.itrs.net/Common/2004Update/2004Update.htm
12	Strategy for Nanotechnology-Related Environmental, Health, and Safety Research	http://www.nanolgov/
13	Nanotechnology - A report of the US FDA Nanotechnology Task Force (FDA)	http://www.fda.gov/nanotechnology/taskforce/report2007.html
14	Prioritization of EHS Research Needs for Engineered Nanoscale Materials - An interim document for public comment (NEHI Working Group)	http://www.nano.gov/Prioritization_EHS_Research_Needs_Engineered_Nanoscale_Materials.pdf
15	Nanomaterials in the workplace - Policy and planning workshop on Occupational Safety and Health (RAND)	http://www.rand.org/pubs/conf_proceedings/2006/RAND_CF227.sum.pdf
16	Vision2020: Joint NNI-CHI CBAN and SRC CWG5 Nanotechnology Research Needs Recommendations	http://www.chemicalvision2020.org/pdfs/chem-semi%20ESH%20recommendations.pdf
17	US EPA Nanotechnology White Paper (EPA)	http://es.epa.gov/ncer/nano/publications/whitepaper12022005.pdf
18	The National Nanotechnology Initiative - Strategic Plan	http://www.nano.gov/html/about/strategicplan.html
19	EHS Research Needs for Engineered Nanoscale Materials	http://www.nano.gov/NNI_EHS_research_needs.pdf
20	Approaches to Safe Nanotechnology: An Information Exchange with NIOSH - Draft for Public Comment (NIOSH)	http://www.cdc.gov/niosh/topics/nanotech/
21	Toxicology steps up to nanotechnology safety	http://www.rdmag.com/
22	Nanotechnology environmental health & safety standards	http://www.iso.org/iso/iso-focus-index
23	Strategic Plan for NIOSH Nanotechnology Research and Guidance	http://www.cdc.gov/niosh/topics/nanotech/strat_plan.html
24	Productive Nanosystems - A technology roadmap	http://www.foresight.org/roadmaps/Nanotech_Roadmap_2007_main.pdf
25	Project on Emerging Nanotechnologies (Research Brief) - A survey of EHS Risk Management Information Needs and Practices among Nanotechnology Firms in the MA Region (Woodrow Wilson Int'l Center for Scholars)	http://www.nanotechproject.org/
26	TSCA Inventory Status of Nanoscale Substances (EPA)	http://epa.gov/oppt/nano/nmsp-inventorypaper.pdf
27	Towards Predicting Nano-Biointeractions: An international assessment of nanotechnology environment, health and safety research needs	http://cohesion.rice.edu/CentersAndInst/ICON/emplibrary/ICON_RNA_Report_Full2.pdf
28	Nanoscale Materials Stewardship Program, Interim Report (EPA)	http://www.epa.gov/oppt/nano/stewardship.htm#report